National Pharmaceutical Pricing Authority

REPORT ON PRICING OF STENTS

The National Pharmaceutical Pricing Authority (NPPA) undertook this study on pricing of stents in pursuance of a request received in this regard from the Department of Pharmaceuticals, Ministry of Chemicals & Fertilizers vide letter no. 31026/ 53/ 2014-PI.I dated 11.12.2014 (copy placed at **Annexure 1**). The background to the abovementioned exercise includes news reports in certain sections of press regarding huge mark-up in prices of stents due to unreasonable margins to distributors and hospitals.

2. It may also be mentioned that in a public interest litigation filed by Shri Birender Sangwan versus Union of India, through Ministry of Health & Family Welfare, and National Pharmaceutical Pricing Authority, New Delhi, (case of w.p.(c) 1772/2015) seeking directions of the court for inclusion of "Coronary Stents" in the National List of Essential Medicines (NLEM), the Hon'ble High Court, Delhi has passed an order on 25.02.2015 directing the respondents , "to treat this petition as a representation and pass an appropriate order in accordance with law within a period of 3 months from today." It also states that the said order shall be communicated to the petitioner and the petitioner is at liberty to avail the appropriate remedies available under law for redressal of the further within a period of 3 months from today (copy of order placed at **Annexure 2**).

3. Further, the matter was also raised in a meeting organised by NPPA with State Drugs Controllers on implementation of Drugs (Prices Control) Order (DPCO) 2013, including revision of the First Schedule to DPCO 2013. The State Drug Controller of Odisha vide letter no. DC-Misc-DPCO-15/06/10211 dated 24.12.2014 has recommended control over the prices of stents under paragraph 19

of the DPCO 2013, as it is not included in the National List of Essential Medicines - 2011(NLEM) and therefore, does not form part of the First Schedule to the DPCO 2013 for the purpose of price control. He has suggested that, in the meanwhile, all manufacturers/ importers of medical devices should be directed to submit information in Form V of Schedule II to the DPCO 2013 for monitoring year-on-year increase in the maximum retail price (MRP) with a view to preventing overcharging. As per DPCO 2013the year-on-year increase in MRP in respect of non-scheduled drugs cannot exceed the 10%. Based on a market survey, he submitted the Price to Distributor and MRP and the Price to Hospital and selling price to patient details with respect to various medical devices, including stents, which shows huge margins being allowed to distributors and hospitals. A copy of the communication received is placed at **Annexure 3**.

4. Similarly, Commissioner, Food and Drug Administration, Maharashtra vide letter no. DPCO/ 353-14/13 dated 19.09.2014 has requested NPPA to fix MRP for 14 medical devices, including Cardiac Stents. The Commissioner, Food and Drug Administration, Maharashtra had earlier vide letter dated 23.08.2011 recommended price fixation in respect of 7 medical devices, including Peripheral Stents. A copy of the communication received in placed at **Annexure 4**.

5. The Ministry of Health and Family Welfare, Government of India has notified the following medical devices as 'Drugs' under Section 3(b) (iv) of the Drugs and Cosmetics Act, 1940, which includes Cardiac Stents (Bare Metal) and Drug Eluting Stents:-

Sl.No.	**Name of the Medical Device**	**Notification number**	**Date**
1	Disposable Hypodermic Syringes	GSR 365(E)	17.03.1989

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Sl.No.	Name of the Medical Device	Notification number	Date
2	Disposable Hypodermic Needles	GSR 365(E)	17.03.1989
3	Disposable Perfusion Sets	GSR 365(E)	17.03.1989
4	In-vitro Diagnostic Devices for HIV, HBsAg and HCV	GSR 601(E)	27.08.2002
5	**Cardiac Stents**	**S.O. 1468 (E)**	**06.10.2005**
6	**Drug Eluting Stents**	**S.O. 1468 (E)**	**06.10.2005**
7	Catheters	S.O. 1468 (E)	06.10.2005
8	Intra-Ocular Lenses	S.O. 1468 (E)	06.10.2005
9	I.V. Cannulae	S.O. 1468 (E)	06.10.2005
10	Bone Cements	S.O. 1468 (E)	06.10.2005
11	Heart Valves	S.O. 1468 (E)	06.10.2005
12	Scalp Vein Set	S.O. 1468 (E)	06.10.2005
13	Orthopaedic Implants	S.O. 1468 (E)	06.10.2005
14	Internal Prosthetic Replacements	S.O. 1468 (E)	06.10.2005

6. In addition to the above, the following products are also regulated as 'Drugs' under the Drugs and Cosmetics Act, 1940 and Rules made thereunder:-

1. Blood Grouping Sera
2. Ligatures, Sutures and Staplers
3. Intra-Uterine Devices (Cu-T) (**Scheduled Drug**)
4. Condoms (**Scheduled Drug**)
5. Tubal Rings
6. Surgical Dressings
7. Umbilical Tapes
8. Blood/ Blood Component Bags

7. Accordingly, at present, Condoms and IUDs are the only two medical devices included in the NLEM and incorporated in the First Schedule to the Drugs (Prices Control) Order (DPCO) 2013 for the purpose of price control, and the remaining are treated as non-scheduled drugs. With respect to non-scheduled drugs, NPPA monitors the annual price movement in order to ensure that the 10% ceiling stipulated in DPCO 2013 on year-on-year increase in MRP is not breached.

8. The number of cardiac interventions in the country has grown more than five-fold during the past 10 years, from around 40,000 in 2006 to nearly 2,20,000 in 2013. Coronary Atherosclerotic Heart Disease (CAD)is a common form of cardiovascular disease in India, which afflicts around 32 million people with a mortality of around 1.6 million per annum. Cardiacstent is specifically used for treatment of coronary artery closure. Nearly 2% of CAD patients are treated with angioplasty. Angioplasty procedure is very common these days, but the high cost of cardiac stents is a major cause of concern, as it seriously affects the ability of the common man to access it. A cardiac stent is a small expandable tube, which is used to treat narrowed or weakened arteries in the body. It is typically made of metal mesh, and implanted in narrowed coronary artery during a procedure called a Percutaneous Coronary Intervention (PCI) or angioplasty. Unlike coronary artery bypass surgery, stenting is minimally invasive because it involves no major incisions.

9. Although NPPA has not fixed the Ceiling Price of Stents because it is a non-scheduled drug, but its price movement has to be monitored by NPPA on the basis of the price list submitted by manufacturers, including importers, in Form V of Schedule II to the DPCO 2013. However, most manufacturers, including importers of medical devices, have either not been submitting the information at all or not submitting it regularly due to which NPPA has issued a show cause notice dated

16.02.2015 to all manufacturers of medical devices, including importers, giving them two weeks' time to submit the information. A copy of the SCN is placed at **Annexure 5**.

10. At the same time, in order to arrive at a reasonable benchmark price for Bare Metal Stent (BMS) and Drug Eluting Stent (DES), NPPA requested the National Health Systems Resource Centre (NHSRC), a technical support institution under Ministry of Health & Family Welfare, the Division of Healthcare Technology to undertake an assessment of clinical effectiveness and cost effectiveness of BMS and DES from affordability angle. A copy of the request letter sent in this regard is placed at **Annexure 6**.An interim report was submitted by NPPA pending NHSRC report.

11. NHSRC conducted a study on pricing of stents and submitted their report to NPPA, a copy of which is placed at **Annexure 7**. The NHSRC report evaluates both Bare Metal Stents (BMS) and Drug Eluting Stents (DES)in terms of clinical-effectiveness and cost-effectiveness. A BMS is a mesh-like tube of thin wire made of stainless steel or cobalt chromium alloy without any drug coating. The stent diameter can range from around 2mm to 4mm, depending on the diameter of the individual vessel, as well as the specific condition and extent of disease. The primary purpose of a stent is to hold the inner wall of the blood vessel in order to remove any obstruction to blood flow. The composite metals differ in degrees of strength and flexibility. Specific materials and designs are used to create greater thrombo-resistance, and to make stents both radio-opaque and biocompatible.

12. Stents eluting anti-mitotic agents are called drug-eluting stents (DES), which help in preventing re-stenosis since they are designed to inhibit growth of new

tissue. Biocompatible polymer stent coatings can be used as a base for binding drugs and other compounds to a stent. Placement of a drug onto a stent with a special polymer coating or positioning a drug-eluting sleeve around a metal stent allows slow drug release over a period of 15-45 days, which also reduces the risk of toxicity.

13. For the sake of better appreciation, some examples of different types of stents and popularly used brands are given in the table below:-

Stent Type	Description	Examples
Drug-eluting stent	A stent that slowly releases a drug to block cell proliferation and/or restenosis	- Cypher (J&J/Cordis) - Taxus (Boston Scientific) - Xience V (Abbott Vascular) - Endeavor (Medtronic)
Bare metal stent, stainless steel	A vascular thin metal wire or mesh stent without a coating, typically first-generation technology	- Bx Velocity (J&J/Cordis) - Express2 (Medtronic) - Millennium Matrix (Sahajanand Medical Technologies)
Bare metal stent, CoCr	A vascular thin metal wire or mesh without a coating, typically next-generation technology	- Driver (Medtronic) - Multi-Link Vision (Abbott Vascular) - Corronnium (Sahajanand Medical Technologies)
Absorbable stent	Completely biodegradable, bioabsorbable stent, typically polymer or magnesium, sometimes coated with anti-restenotic agent	- AMS (Biotronik) ABSORB trial (Abbott Vascular) - REVA/RESORB trial (REVA Medical)
Bioactive stent	A stent that reacts with the body's natural processes to achieve an anti-restenotic effect	- Genous (OrbusNeich) - Titan2 BAS (Hexacath)
Radioactive stent	Stent with a radiation-emitting coating	- (Name undisclosed) (MoBeta, Inc.)
Drug-eluting balloon	Angioplasty balloon that, after deflation, leaves behind an anti-restnotic drug	- SeQuent Please (B. Braun Melsungen) - DIOR (EuroCor) - Elutax (Aachen Resonance)

14. The objectives of the Health Technology Assessment of Cardiac Stents conducted by NHSRC were as follows:-

i. To assess the clinical effectiveness of DES and BMS across three major outcomes- mortality, revascularization and major adverse cardiac events.
ii. To estimate the price of BMS and DES categories of cardiac stent, at which it would be cost effective for patients in Indian context.

15. The methodology adopted by NHSRC includes literature search for evidence on clinical effectiveness of cardiac stents, as per a pre-defined selection criteria and inclusion criteria. Based on a thorough and systemic analysis of literature on the subject matter, outcomes with respect to Mortality, MACE (major adverse cardiac events), and Target Vessel Revascularisation (TVR) were relied upon to arrive at conclusions on the effectiveness of the two types of stents (BMS and DES).

16. The three outcomes were not necessarily primary outcomes in all studies, but were certainly one or more of the outcomes reported therein. The gist of the comparative effectiveness assessment of BMS and DES as per the NHSRC study are given below:-

(i) As per findings, DES is 1.52 times more effective from a perspective of reduction in number of major adverse cardiac event as compared to BMS.

(ii) As per the analysis, there is 27% reduction in incidence of mortality by the use of DES compared to BMS; also meaning that DES is 1.37 times more effective in reducing mortality within one year of angioplasty.

(iii) As per the findings, there is 35% reduction in incidence of TVR (Target Vessel Revascularisation) by the use of DES compared to BMS, which also means that DES is 1.54 times more effective in reducing the TVR events.

(iv) Overall, taking all the three parameters into consideration, DES is 1.476 TIMES more effective than BMS

17. Based on these findings, the study assessed the cost-effectiveness of DES and BMS using Quality Adjusted Life Years (QALYs)/ Disability Adjusted Life Years (DALYs) approaches. QALY relates to both the quantity and quality of life generated by healthcare interventions. QALY assumes that a year of life lived in perfect health is worth 1 QALY and that a year of life lived in a state of less than this perfect health is worth less than 1. Similarly, DALY is a measure of the number of years lost due to ill-health, disability or early death. DALYs are calculated by taking the sum of Years of life lost (YLL) and Years of life lived with disability (YLD).

18. The World Health Organisation CHOICE (Choosing Interventions that are Cost Effective) measures cost-effectiveness using Gross Domestic Product (GDP) as the indicator. Under the methodology adopted by WHO the affordability of stents is assessed in terms of1 DALY as a percentage of per capita income. Based on the abovementioned methodology used by the WHO, stents can be grouped under three categories, namely, highly cost-effective; cost-effective; and not cost-effective as given below:-

- Highly cost-effective < less than one GDP per capita;
- Cost-effective: between one and three times GDP per capita; and
- Not cost-effective > more than three times GDP per capita

19. Taking into account the CAD burden in the country in different sub-categories (Ischemic heart disease, Stroke and other circulatory diseases)in different age-groups (30-59; 60-69; and 70+ years), duly factoring therapeutic

effectiveness of DES vis-a-vis BMS, the study, assuming that in about 60% of cases the treatment would require implant of cardiac stents, and the DALYs lost for the remaining 40% of DALYs would still be lost; the total DALYs averted for the 60% of cases was worked out as 0.062 DALYs/per person averted. on this, the DALYs/ per person averted multiplied by the WHO formula (up to 3 times GDP per capita), taking the GDP at US$ 1500 per capita, and adding 12.36% hospital handling charges (including service tax), the report arrives at a cost-effective BMS price of Rs. 19,000/- and Rs. 28,000/- for DES.

20. When the abovementioned benchmark prices are juxtaposed against the maximum retail price (MRP) of popularly sold brands of BMS and DES, which is what is normally charged to the patient, it is seen that, in the absence of stent price regulation in the country, there is a huge exploitation of the consumer due to extreme overpricing stents of sold in the country, especially imported brands, making it out of reach for majority of the people suffering from CAD, and also impoverishing those who cannot afford it but are compelled to incur catatrophic medical expenditure for the treatment purposes.

21. Based on analysis of the information submitted by manufacturers/ importers of Stents, it is seen that there is unreasonable mark-up in the final cost to the patient when compared with the ex-factory cost or landed cost, as the case may be. It is seen that bulk of stents consumed in the country are imported, and the maximum retail price (MRP) in many cases is ten times the landed cost, the bulk of which is accounted for by distributor/ hospital margins and promotional expenses. The information submitted by major manufacturers is placed at **Annexure 8**; and the analysis done on the basis of information received is placed at **Annexure 9A**

and 9B, and an international price comparison done by NHSRC is given at **Annexure 9C**.

22. Annexure 9A contains the prices of 9 companies, including those of market leaders such as Abbott, Medtronic and Boston Scientific that together account for nearly 60% of the market share of stents in the country. In the case of Abbott, the difference between landed cost (LC) and price to distributor (PTD) ranges between 68% to 140% across different brands; that between PTD and MRP ranges between 72% to 400%; and finally between LC and MRP ranges between 294% to 740%. Abbott makes institutional supply to CGHS with a margin of 100% to 200% only. This indicates the quantum of margin in the distribution channel, which is totally detrimental to consumer interest. In the case of Medtronics, the margin between LC and PTD ranges between 82% to 232%across different brands; that between PTD and MRP ranges between 170% to 325%; and finally that between LC and MRP ranges between 498% to 854%. Similarly, in the case of Boston Scientific, the margin between 43% to 105% across different brands; that between PTD and MRP ranges between 175% to 809%; and finally that between LC and MRP ranges between 464% to 1200%.

23. Annexure 9B gives the maximum and minimum LC, PTD and MRP, and the margins in respect of Stents across different manufacturers and brands, which is as under:-

Rs/ Landed Cost	PTD	MRP	%PTD/LC	%MRP/PTD	% MRP/LC
Maximum	**50,257**	**1,15,000**	**1,98,000**	**232**	**1,086**	**1,207**
Minimum	**2,968**	**2,806**	**7,000**	**- 20**	**66**	**103**
Average						
Arithmetic Mean	**12,931**	**28,017**	**1,04,966**	**93**	**346**	**783**
Median	**12,648**	**28,452**	**1,27,000**	**115**	**334**	**825**
Mode	**12,648**	**6,497**	**1,50,000**	**136**	**100**	**1,086**

24. Annexure 9C gives a comparative analysis of prices of Stents of a few brands across countries – UK, US and India. It is seen that there is not much differnece in prices in dollar terms, but in terms of affordability, including in terms of PPP, the prices of Stents in India are very high when compared with the UK and the US. In PPP terms it is more than 10 times costlier in India as compared to the UK and the US. This is a cause of deep concern, as only 60% of cases are covered by Government (45%)/ Private insurance (15%). In the remaining 40% cases, the cost is being met by way of out-of-pocket expenses.

25. While it is difficult to state in exact terms the total market of stents in India in the absence of a comprehensive registry in place for this purpose, the current market size for stents in the country as per Interventional Council of India is 2.62 lakh (2013), out of which the share of DES is 78%. The consumption of stents in the country has risen from 1,46,719 in 2010 to 2,62,349 in 2013, which indicates how rapidly the market is growing. The market is currently growing at a rate of around 15% every year and is poised to become the second largest market after China by 2020. Currently, the market is dominated imported stents manufactured by multinational companies such as Abbot (26.4%), Medtronic (22.46%), Meril Life Sciences (11.90%), Vascular Concepts (8.46%), and Boston Scientific (8.34%). Sahajanand, an Indian company, accounts for 5.10%. Others manufacturers include ATL Therapeutics, Biosensors, Vasmed, Choksy, MIC, Lancer, Cordis, B Braun, Optocircuit, IBM, Biotronik, Heartbeat, etc. The dominant players determine the market dynamics related to price points and product promotion activities, but they are hugely influenced by the dictates of major coronary centres performing coronary interventions. Here again the market is highly concentrated with 44% of angioplasty done in the country by 54 centres, which represents 13% of the total of 404 centres. Unlike India, where more than

three-fourth of stents used are imported, in China, bulk of the stents used are indigenously manufactured. Though standard Indian stent brands are far more economical compared to popular imported brands, and they fully meet international specifications, the demand for them is very low, which may be attributed to steep information asymmetry and aggressive promotional practices of big companies, which does not enable the patient to make an informed decision.

26. Some of the typical challenges with respect to choice of stents, which have had a distorting effect on the market, and recommendations to address those concerns are enumerated below:-

i. Patients are often deprived the opportunity of understanding the difference between different types/ qualities of Stents, and as a result their choice is governed almost entirely by the cardiologist's recommendations. It is necessary to educate patients about the treatment, including various options along with therapeutic value and cost implication. Every Hospital must display outside the Cath Lab the Stents available with the Hospitals along with their MRP.

ii. In most cases, the patient is given negligible time to decide on the choice of Stent, as the physician expects instant decision at the time of angiography procedure itself. Under such circumstances, the decision-maker is left with no alternative but to accept whatever is recommended by the doctor. It is desirable to adequately prepare the patient and give him time to decide unless it is an emergency case.

iii. The common public perception/ belief that imported stents are superior to Made-in-India Stents though it is not supported with any clinical validations should be demolished through proper information dissemination. Unfortunately, many hospitals, including Government hospitals, are creating special categories on the basis of country-specific regulator-approvals such as USFDA approved DES(American) CE mark DES(European) and DCGI approved DES (Indian) in their tenders for purchase of DES, which encourages perceptions that products approved by a particular regulator is of higher quality based on the price band. This is typical in the pharma sector where higher price is often confused with 'higher quality'. Hence, such categorisation is not at all desirable, and all tenders should be floated on the basis of specifications and not specific country-approvals. It may be noted that such categorisation restricts competition, as many Indian manufacturers who even export stents to EU countries are unable to compete due to such exclusive categorisation, as they may not have USFDA approval, which leads to overpricing. This should be rectified so as to enable competition among all manufacturers (Indian, European, American and others) based on technical and other specifications.

iv. Recently the Ministry of Health & Family Welfare has circulated a proposal for amendment to the Drugs & Cosmetics Act, 1940 in which, inter alia, it has been proposed to remove medical devices from the definition of drugs. The effect of this amendment of the definition of "Drugs" so as to exclude the "medical devices" will be that medical devices will no more be under DPCO, 2013 as the DPCO can apply only to drugs. Once, the definition of the Drugs under the Drugs and Cosmetics Act is amended to exclude medical devices, all the medical devices including Cardiac Stent viz. BMS

and DES will be out of any regulation of the Essential Commodities Act and the Drugs (Price Control) Order issued thereunder. If decided for such a legislation, it is suggested that an appropriate mechanism should be placed so that license and permission to manufacture and market medical devices including cardiac stents is issued by the Central Licensing Authority as in the case of category of "New Drugs" under Drugs and Cosmetics Act. The central authority should also differentiate the current generation of DESs on the basis of clinical data and quality for promoting value-based pricing.

v. Simultaneously, Medical Council of India (MCI) should also come out with standard procedural guidelines, specific to each medical device including cardiac stents that puts a check on the entire proceedings from the initial stage of admission till patient is discharge after implantation of medical device.

vi. The margin for distributor/importer/supplier and hospitals should be regulated in order to keep the price of DES and BMS at reasonable level.

27. **Conclusion:** The issues flagged and recommendations made in paragraph 26 above may be considered by Ministry of Health and Family Welfare for appropriate measures in this regard.

Ministry of Health & Family Welfare has recently circulated draft of "The Drugs and Cosmetics (Amendment) Bill, 2015 to further amend the Drugs and Cosmetics Act, 1940. The proposed amendment Bill primarily provides for separate provisions for "medical devices" distinct from "drugs" and also for "clinical trials.". NPPA, while giving its comments to DoP on the proposed amendments, had very clearly emphasised that Ministry of Health and Family

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Welfare may like to elaborate as to who will regulate the medical device market and how.

Since the amendment to the Drugs & Cosmetics Act, as proposed by the Ministry of Health & Family Welfare will take some time; in fact the Amendment Bill has not even been placed before the Cabinet, therefore it is imperative to take certain steps in the meanwhile.

With respect to price regulation of stents, it is suggested that all types of Stents, including BMS and DES, may be included in the NLEM. And pending such inclusion in the NLEM and incorporation in Schedule-I of DPCO, 2013, price fixation under para 19 of the DPCO, 2013 for regulating the MRPs of cardiac stents, may be considered in consultation with Department of Health in view of the proposed exclusion of medical devices from the definition of "Drug" as per draft bill for amendment in the Drugs & Cosmetics Act, 1940. The three requirements of paragraph 19 are fully met in the case of stents. The ignorance of the consumer coupled with highly exploitative pricing (as explained in paragraphs 22 to 24 above) is resulting catastrophic medical expenditure and impoverishment of the patient and her/ his family in a large number of cases, which constitutes the extraordinary circumstances for proposed intervention under paragraph 19; the exploitative pricing of stents makes it out of reach for majority of patients, and, therefore, in order to protect public interest and make coronary interventions involving implant of Stents affordable, it becomes necessary to regulate the current irrational margins allowed to the distributors and Hospitals and promotional costs incurred; and finally in the light of the fact that stents are not currently in the NLEM/ First Schedule to the DPCO 2013 for the purpose of price control, it becomes imperative to regulate the prices of Stents under paragraph 19 of the DPCO 2013.